REMARKS/ARGUMENTS

Reconsideration and continued examination of the above-identified application are respectfully requested.

By way of this amendment, claims 1-33 have been canceled without prejudice or disclaimer. New claims 34-41 have been added. Full support for new claims 34-41 can be found at least in originally filed claims 14 and 33, as well as paragraphs [0003], [0005], [0041], [0046], [0048]-[0050], [0081]-[0083], [0085] and [0091] of the present specification. The new claims are part of the elected invention, as they are drawn to methods of identifying a compound having an effect of enhancing expression and/or function of sFRP and methods of identifying a compound that inhibits tumor formation. The applicant reserves the right to pursue the non-elected claims in one or more divisional applications. Accordingly, no questions of new matter should arise and entry of the amendment is respectfully requested.

Rejection of claims 13-15 and 33 under 35 U.S.C. §112, second paragraph

At pages 2-11 of the Office Action, the Examiner rejects claims 13-15 and 33 under 35 U.S.C. §112, first paragraph. The Examiner states that the specification, while disclosing *Dlg* heterozygous (+/-) and homozygous (-/-) knockout mice, does not reasonably provide enablement for providing a genus of heterozygous *dlg* gene knockout non-human mammals. Accordingly, the Examiner states that the claims are only enabled for mice.

The Examiner also states that the specification does not reasonably provide enablement for identifying a compound having an effect of enhancing the expression and/or function of either *Dlg* or sFRP or a compound that inhibits tumor formation in a *Dlg* +/- animal or cells from the animal. The Examiner further states that according to the specification, tumor formation was

due to lack of *Dlg* gene in tumor cells. As such, the Examiner concludes that, short of restoring the *Dlg* gene, it is unlikely that a compound could enhance *Dlg* expression or function when an allele of the gene is missing, and that it is unlikely that any compound could inhibit tumor formation due to the deficient *Dlg* gene. This rejection is respectfully traversed.

Claims 13-15 and 33 have been canceled. The applicants provide the following comments in view of new claims 34-41 which are part of the elected invention. In addition, in order to further assist the Examiner, the Applicants provide a Declaration under 37 CFR 1.132 of the named inventors that includes information and data with specific information regarding experiments performed.

New claims 34-41 comply with the requirements of 35 U.S.C. §112, first paragraph.

New claims 34-41 recite methods for identifying a compound which comprise, in part, using a mouse that is deficient in both of Dlg alleles or a cell originating in a mouse that is deficient in both of Dlg alleles. The present application states that a compound having an effect of enhancing the expression and/or function of Dlg can be identified by administering a compound to to a Dlg gene deficient non-human mammal, and measuring the expression and/or function of Dlg in the mammal (paragraph [0078]). As the Examiner stated, the specification describes homozygous Dlg (-/-) knockout mice (e.g. paragraphs [0041], [0044], and [0046]). Further, the present application states that the method of identifying a compound according to the present invention can be conducted using a cell originating in a Dlg gene deficient non-human mammal, such as a mouse (paragraphs [0091] and [0093]). Thus, the specification does provide enablement for identifying a compound by using a mouse that is deficient in both of Dlg alleles or a cell originating in a mouse that is deficient in both of Dlg alleles.

New claim 34 is directed to a method of identifying a compound having an effect of

enhancing expression and/or function of sFRP (secreted frizzled-related protein), comprising: a) using a mouse that is deficient in both of Dlg alleles; b) administering a test compound to the mouse; and c) measuring expression and/or function of sFRP. New claim 35 is directed to a method of identifying a compound having an effect of enhancing expression and/or function of sFRP, comprising: a) using a cell originating in a mouse that is deficient in both of Dlg alleles; b) contacting a test compound with the cell; and c) measuring expression and/or function of sFRP. New claims 36 and 37 are dependent on new claims 34 and 35, respectively.

Regarding new claims 34-37, as noted by the Examiner, the specification teaches that Dlg -/- mice show reduced or missing gene expression of sFRP1 and sFRP2, respectively (e.g. paragraph [0046]). The present application describes that the present identification method comprising measuring the expression and/or function of sFRP identifies a compound having an effect of enhancing the expression and/or function of sFRP (paragraph [0081]). The present application states that when it is found that the amount of expression of sFRP in a Dlg gene deficient non-human mammal subjected to administration of a test compound is increased compared to that in a Dlg gene deficient non-human mammal not subjected to administration of the test compound, it can be determined that the test compound has an effect of enhancing the expression of sFRP (paragraph [0082]). The present application also states that when it is found that the function of sFRP in a Dlg gene deficient non-human mammal subjected to administration of a test compound is increased compared to that in a Dlg gene deficient non-human mammal not subjected to administration of the test compound, it can be determined that the test compound has an effect of enhancing the function of sFRP (paragraph [0083]). Further, the present application states that the method of identifying a compound according to the present invention can be conducted using a cell originating in a Dlg gene deficient non-human mammal

(paragraph [0091]). Thus, the specification does provide enablement for identifying a compound having an effect of enhancing expression and/or function of sFRP by using a mouse that is deficient in both of Dlg alleles or a cell originating in a mouse that is deficient in both of Dlg alleles.

In addition, the present application describes mechanisms by which Dlg can affect expression of sFRP (paragraph [0050]). Further, as stated in the Declaration under 37 C.F.R. §1.132, expression of sFRP2 in Dlg -/- cells was increased by over-expression of Runx1. This result indicates that a compound having an effect of enhancing expression and/or function of Runx can enhance sFRP expression in a cell lacking both Dlg alleles. The method claimed in new claim 34-37 can provide such a compound that works on molecules involved in the signal transduction pathway downstream of Dlg to enhance expression and/or function of sFRP.

Thus, the present application does provide enablement for identifying a compound having an effect of enhancing expression and/or function of sFRP by using Dlg -/- mice or Dlg-/- cells.

New claim 38 is directed to a method of identifying a compound that inhibits tumor formation, comprising:

a) using a mouse that is deficient in both of Dlg (discs large) alleles;

b) administering said compound to the mouse; and

c) measuring expression and/or function of sFRP.

New claim 39 is directed to a method of identifying a compound that inhibits tumor formation, comprising:

a) using a cell originating in a mouse that is deficient in both of Dlg alleles;

b) contacting said compound with the cell; and

c) measuring expression and/or function of sFRP.

New claims 40 and 41 are dependent on new claims 38 and 39, respectively.

Regarding new claims 38-41, the present application teaches that a compound having an effect of enhancing expression and/or function of sFRP can inhibit tumor formation, and that a compound that inhibits tumor formation can be provided by identifying a compound having an effect of enhancing expression and/or function of sFRP. In particular, the present application describes that sFRP binds to Fz and Wnt outside a cell and works as an antagonist of the Wnt signal, and thereby participates in regulation of the Wnt signal (paragraph [0005]). In addition, the present application describes that the Wnt signal was found as a signal transduction system involved in regulation of morphogenesis, and is known to participate in numerous events including development, regulation of stem cell differentiation, and tumor formation (paragraph [0003]). Furthermore, the present application describes that a compound having an effect of enhancing the function of sFRP may be a compound having an effect of inhibiting tumor formation (paragraph [0085]). Further, the present application describes that it was reported that restoration of the function of sFRP family such as sFRP2 in a colorectal cancer cell induced reduction of the Wnt signal (paragraph [0048]), and states that the mechanism of tumor formation due to Dlg gene deficiency can be considered to include a cascade in which the reduced expression and/or function of sDlg inhibits the expression and/or function of sFRP resulting in an increase of the Wnt signal (paragraph [0049]).

Furthermore, as described above, the present application does provide enablement for identifying a compound having an effect of enhancing expression and/or function of sFRP by using Dlg -/- mice or Dlg-/- cells.

Thus, the present application does provide enablement for identifying a compound that inhibits tumor formation by identifying a compound having an effect of enhancing expression

and/or function of sFRP in Dlg -/- mice or Dlg-/- cells.

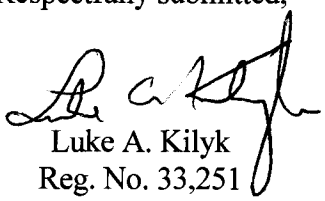
Accordingly, the claims satisfy 35 U.S.C. §112 and the rejection should be withdrawn.

CONCLUSION

In view of the foregoing remarks, the applicant respectfully requests the reconsideration of this application and the timely allowance of the pending claims.

If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0925. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such extension is requested and should also be charged to said Deposit Account.

Respectfully submitted,



Luke A. Kilyk
Reg. No. 33,251

Atty. Docket No. 3190-101
KILYK & BOWERSOX, P.L.L.C.
400 Holiday Court, Suite 102
Warrenton, VA 20186
Tel.: (540) 428-1701
Fax: (540) 428-1720
Attachment: Declaration under 37 C.F.R. §1.132 (7 pages)